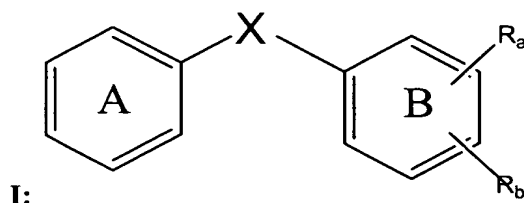


CLAIMS

What is claimed is:

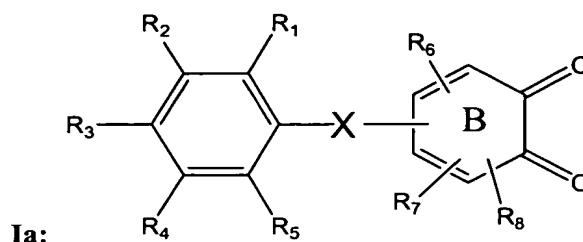
1. A composition which selectively reduces blood flow to a tumor region and forms a
 5 ROS *in vivo*, wherein said composition comprises an anticancer agent having a quinone, quinone prodrug, catechol or catechol prodrug moiety, provided that said composition is not combretastatin A-1 or a salt, ester or prodrug thereof.
2. The composition of claim 1 wherein said moiety is in the *ortho* position.
3. The composition of claim 1 wherein said anticancer agent is a tubulin binding agent.
- 10 4. A compound comprising the structure of formula I:



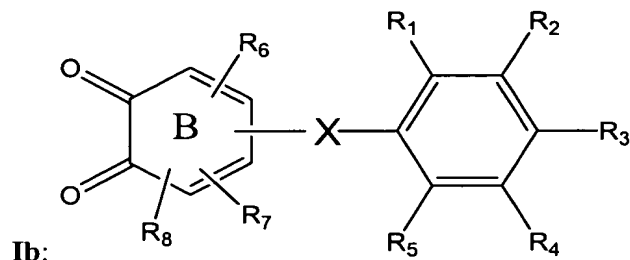
wherein:

- Ring A is optionally substituted with one to five substituents selected from
 - 15 a) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - b) a halogen or trihaloalkyl;
 - c) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - 20 d) an OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - e) NH₂ or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- f) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;
- 5 - Ring B comprises at least one structure denoted by R_a and R_b , which represent an *ortho*-quinone moiety $-(C=O)-(C=O)-$, *ortho*-catechol moiety $-(C-OH)-(C-OH)-$ or *ortho*-catechol pro-drug moiety $-(C-O-Prodrug\ moiety)-(C-O-Prodrug\ moiety)-$; and the remaining carbons of Ring B are optionally substituted with one to five substituents selected from
- g) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- 10 h) a halogen or trihaloalkyl;
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- j) OH or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
- 15 k) NH_2 or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- l) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- 20 - Bridge X is selected from the group consisting of alkenes $-(CR_9=CR_{10})-$, alkanes $-(CR_9-CR_{11}R_{12})$, alkynes, amides $-(NR_9-CO)-$, amines $-(NH-$, $-NR_8-$, or $-CR_9-N-$), carbonyl $-(CO)-$, ethers $-(C\ R_8-O)-$, sulfonamides $-(NR_8-SO_2)-$, sulfonates $-(O-SO_2)-$, aryls, oxo $-(O-$ or $-O\ R_8)-$, thio $-(S-)$, cycloalkyls, propanones $-(C=O)-CR_8=CR_9-$, sulfonamides $-(NR_8-(S=O)_2)-$, and sulfonates $-(O-(S=O)_2)-$; wherein R_8 , R_9 , R_{10} , or R_{11}
- 25 are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy;
- provided that said compound is not combretastatin A1 or a salt, ester, or prodrug thereof.
5. A compound comprising a quinone, quinone prodrug, or a pharmaceutically acceptable salt form thereof having one of the following general structures: /



or



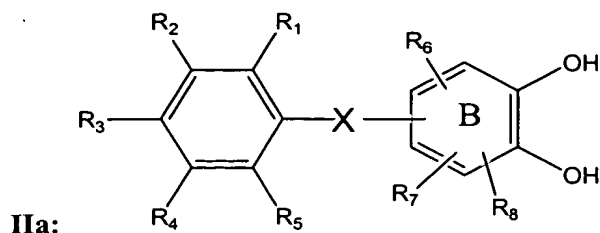
wherein:

- a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from
 - i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;
 - vi) an oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

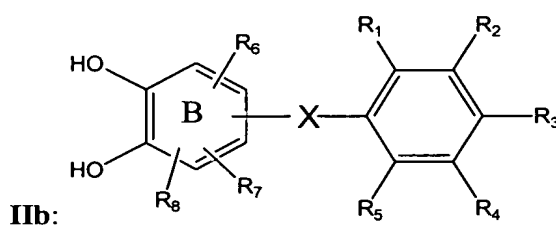
and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

- b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₁R₁₂), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₈-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₈-O-), sulfonamides (-NR₈-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₈-), thio (-S-) cycloalkyls, propanones (-(C=O)-CR₈=CR₉-), sulfonamides (-NR₈-(S=O)₂-), and sulfonates (-O-(S=O)₂-); wherein R₈, R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy.
6. The compound of claim 5, wherein X forms a covalent linkage between Ring A and B comprising two contiguous atoms of the same or different element.
7. The compound of claim 6, wherein the covalent linkage is an ethylene group (-CH=CH-) and Rings A and B are in a cis (Z) isomeric configuration.
8. The compound of claim 7, wherein R₂, R₃, and R₄ are methoxy.
9. The compound of claim 5, wherein said quinone is a bioreductive agent which is reductively activated *in vivo* to form a catechol capable of participating in a redox cycling reaction to form one or more Reactive Oxygen Species ("ROS").

10. A compound comprising a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof having one of the following general structures:



or



wherein:

- a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are selected from
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;

vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, heterocyclo;

and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

- 5 b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₀R₁₁), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₉-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₉-O-), sulfonamides (-NR₉-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₉-), thio (-S-) cycloalkyls, propanones (-C(=O)-CR₉=CR₁₀-), sulfonamides (-NR₉-(S=O)₂-), and sulfonates (-O-(S=O)₂-);
10 wherein R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy;

provided that said compound is not combretastatin A1 or a salt, ester, or prodrug thereof.

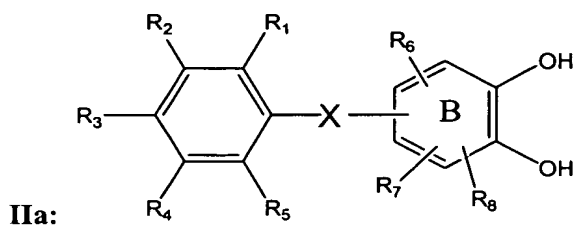
11. The compound of claim 10, wherein X forms a covalent linkage between Ring A and B, comprising two contiguous atoms of the same or different element.
12. The compound of claim 11, wherein the covalent linkage is an ethylene group (-CH=CH-), and Rings A and B are in a cis (Z) isomeric configuration.
15
13. The compound of claim 12, wherein R₂, R₃, and R₄ are methoxy.
14. The compound of claim 13, wherein R₈ is selected from
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - 20 ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - 25 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido;

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

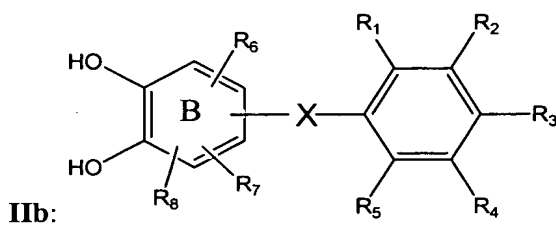
and the remaining R₁, R₅, R₆ and R₇ are H.

- 5 15. The compound of claim 14, wherein R₈ is OH or -O-CH₂-CH=CH₂.
16. The compound of claim 4, wherein said catechol is a biooxidative agent which is oxidatively activated *in vivo* to form a quinone capable of participating in a redox cycling reaction to form one or more Reactive Oxygen Species ("ROS").
- 10 17. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal an antiproliferative agent capable of forming a Reactive Oxygen Species.
18. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a composition which selectively reduces blood flow to a tumor region and forms a ROS *in vivo*, wherein said composition comprises an anticancer agent having a quinone, quinone prodrug, catechol or catechol prodrug moiety.
- 15 19. The method of claim 18, wherein said reduced tumor blood flow is reversible.

20. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof having one the following general structures:



or



wherein:

- 10 a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from
 - i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - 15 iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
 - v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido,

20 lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

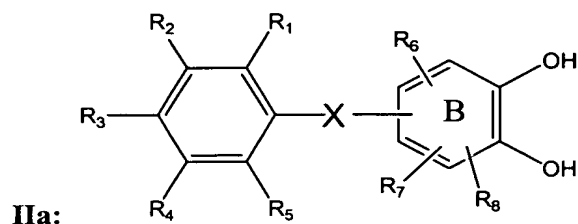
and the remaining R₁, R₂, R₃, R₄, R₅, R₆, R₇, or R₈ are H; and

- 5 b. X is selected from the group consisting of alkenes (-CR₉=CR₁₀-), alkanes (-CR₉-CR₁₀R₁₁), alkynes, amides (-NR₉-CO-), amines (-NH-, -NR₉-, or -CR₉-N-), carbonyl (-CO-), ethers (-C R₉-O-), sulfonamides (-NR₉-SO₂-), sulfonates (-O-SO₂-), aryls, oxo (-O- or -O R₉-), thio (-S-) cycloalkyls, propanones (-C(=O)-CR₉=CR₁₀-), sulfonamides (-NR₉-(S=O)₂-), and sulfonates (-O-(S=O)₂-); wherein R₉, R₁₀, or R₁₁ are alternatively H, alkyl, amino, amido, cyano, hydroxyl, 10 or carboxy.
21. The method of claim 20, wherein X forms a covalent linkage between Ring A and B comprised of two contiguous atoms of the same or different element.
22. The method of claim 21, wherein the covalent linkage is an ethylene group (-CH=CH-) and Rings A and B are in a cis (Z) isomeric configuration.
- 15 23. The method of claim 22, wherein R₂, R₃, and R₄ are methoxy.
24. The method of claim 23, wherein R₈ is selected from
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- 20 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, 25 arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; and
- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; or

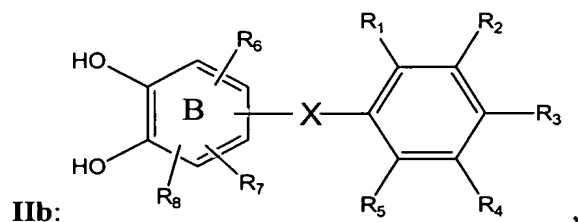
and the remaining R_1 , R_5 , R_6 and R_7 are H.

25. The method of claim 24, wherein R_8 is OH or $-O-CH_2-CH=CH_2$.

26. A method of reducing blood flow in a patient suffering from a vascular proliferative disorder, comprising administering to the patient an effective amount of a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of one the following general structures:



or



wherein:

a. at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are the same or different and are optionally selected from

- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;

- v) NH_2 , or an amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- 5 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;
- and the remaining R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , or R_8 are H; and
- b. X is selected from the group consisting of alkenes ($-\text{CR}_9=\text{CR}_{10}-$), alkanes ($-\text{CR}_9-\text{CR}_{10}\text{R}_{11}$), alkynes, amides ($-\text{NR}_9-\text{CO}-$), amines ($-\text{NH}-$, $-\text{NR}_9-$, or $-\text{CR}_9-\text{N}-$), carbonyl ($-\text{CO}-$), ethers ($-\text{C R}_9-\text{O}-$), sulfonamides ($-\text{NR}_9-\text{SO}_2-$), sulfonates ($-\text{O}-\text{SO}_2-$), aryls, oxo ($-\text{O}-$ or $-\text{O R}_9-$), thio ($-\text{S}-$) cycloalkyls, propanones ($-(\text{C}=\text{O})-\text{CR}_9=\text{CR}_{10}-$), sulfonamides ($-\text{NR}_9-(\text{S}=\text{O})_2-$), and sulfonates ($-\text{O}-(\text{S}=\text{O})_2-$); wherein R_9 , R_{10} , or R_{11} are alternatively H, alkyl, amino, amido, cyano, hydroxyl, or carboxy.
- 10
- 15 27. The method of claim 26, wherein X forms a covalent linkage between Ring A and B comprised of two contiguous atoms of the same or different element.
28. The method of claim 27, wherein the covalent linkage is an ethylene group ($-\text{CH}=\text{CH}-$) and Rings A and B are in a cis (Z) isomeric configuration.
29. The method of claim 28, wherein R_2 , R_3 , and R_4 are methoxy.
- 20 30. The method of claim 29, wherein R_8 is selected from
- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- iii) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- 25 iv) OH , or a C_1 , C_2 , C_3 , C_4 or C_5 primary, secondary, or tertiary alcohol;
- v) NH_2 , amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido,

arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo;

5 and the remaining R_1 , R_5 , R_6 and R_7 are H.

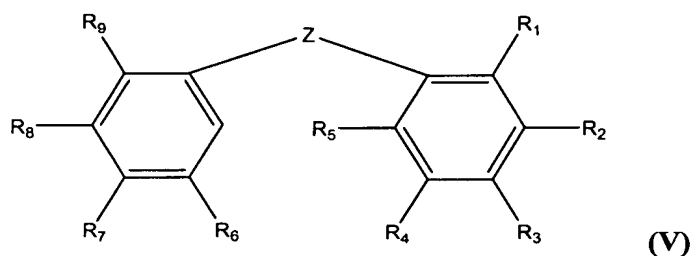
31. The method of claim 30, wherein R_8 is OH or $-O-CH_2-CH=CH_2$.

32. The method of claim 26, wherein said vascular proliferative disorder is selected from the group consisting of solid tumor cancer, wet age-related macular degeneration, diabetic retinopathy, retinopathy of prematurity, diabetic macular edema, uveitis, corneal neovascularization, psoriasis, rheumatoid arthritis, atheroma, restenosis, Kaposi's sarcoma, haemangioma, and inflammatory diseases characterized by vascular proliferation.

10

33. The method of claim 26, wherein the blood flow reduction causes the occlusion, destruction, or damage of proliferating vasculature.

34. A composition of the following formula (V):



15

wherein

- a. Z is an ethylene ($-CH=CH-$) bridge in the cis (Z) isomeric configuration;
- b. R_1 and R_2 are OH or a prodrug form thereof;
- c. at least one of R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , and R_9 are optionally

20

- i) a C_1 , C_2 , C_3 , C_4 or C_5 branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;

- 5 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, aralkanoylamido; or
- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- 10 the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.

35. The composition of claim 34, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.

36. The composition of claim 35, wherein R₆, R₇, and R₈ are the same.

15 37. The composition of claim 36, wherein R₆, R₇, and R₈ are methoxy.

38. The composition of claim 37, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- 20 iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- 25 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- R₄, R₅, and R₉ are hydrogen.

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39. The composition of claim 38, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

40. The composition of claim 39, wherein R₆, R₇, and R₈ are F.

5 41. The composition of claim 40, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, lower alkanoyloxy;
- ii) a halogen or trihaloalkyl;
- 10 iii) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
- iv) OH, or a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) primary, secondary, or tertiary alcohol;
- v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, 15 arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
- vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and

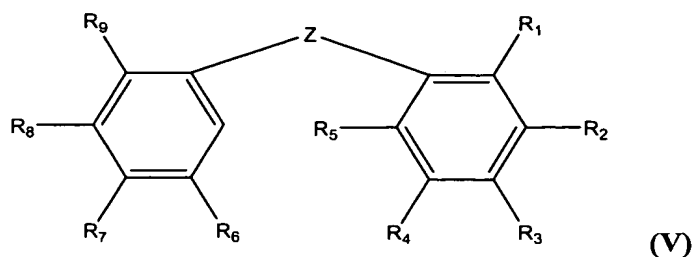
R₄, R₅, and R₉ are hydrogen.

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42. The composition of claim 41, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

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43. A method of inhibiting the proliferation of tumor cells, comprising administering to a mammal a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of formula (V):



5 wherein

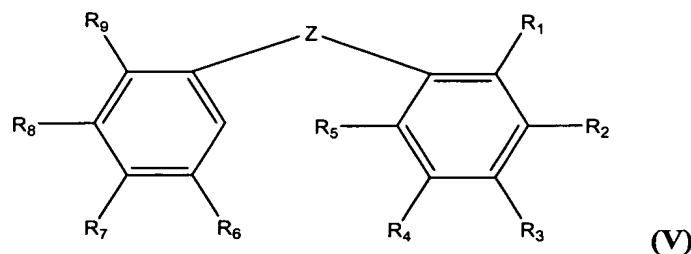
- a. Z is an ethylene (-CH=CH-) bridge in the cis (Z) isomeric configuration;
 - b. R₁ and R₂ are OH or a prodrug form thereof;
 - c. at least one of R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are optionally
 - i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - 15 v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
 - d. the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.
44. The method of claim 43, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.
45. The method of claim 44, wherein R₆, R₇, and R₈ are the same.
46. The method of claim 45, wherein R₆, R₇, and R₈ are methoxy.

47. The method of claim 46, wherein R₃ is

- i) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - 5 iii) a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ (preferably C₁) primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - 10 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- 15 R₄, R₅, and R₉ are hydrogen.

48. The method of claim 47, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.

20 49. A method of reducing blood flow in a patient suffering from a vascular proliferative disorder, comprising administering to the patient an effective amount of a catechol, catechol prodrug, or a pharmaceutically acceptable salt form thereof of formula (V):



wherein

- a. Z is an ethylene (-CH=CH-) bridge in the cis (Z) isomeric configuration;

- b. R₁ and R₂ are OH or a prodrug form thereof;
- c. at least one of R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are optionally
- i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - 5 ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or
 - 10 vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and
- d. the remaining R₃, R₄, R₅, R₆, R₇, R₈, and R₉ are hydrogen.
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50. The method of claim 49, wherein at least three of R₆, R₇, R₈, and R₉ are not hydrogen.
51. The method of claim 50, wherein R₆, R₇, and R₈ are the same.
52. The method of claim 51, wherein R₆, R₇, and R₈ are methoxy.
53. The method of claim 52, wherein R₃ is
- 20 i) a C₁, C₂, C₃, C₄ or C₅ branched or straight-chain lower alkoxy, cycloalkoxy, heterocycloalkoxy, aryloxy, or lower alkanoyloxy;
 - ii) a halogen or trihaloalkyl;
 - iii) a C₁, C₂, C₃, C₄ or C₅ branched or straight chain lower alkyl, allyl, allyloxy, vinyl, or vinyloxy;
 - 25 iv) OH, or a C₁, C₂, C₃, C₄ or C₅ primary, secondary, or tertiary alcohol;
 - v) NH₂, amino, lower alkylamino, arylamino, aralkylamino, cycloalkylamino, heterocycloamino, aroylamino, aralkanoylamino, amido, lower alkylamido, arylamido, aralkylamido, cycloalkylamido, heterocycloamido, aroylamido, or aralkanoylamido; or

vi) oxo, lower alkanoyl, thiol, sulfonyl, sulfonamide, nitro, nitrosyl, cyano, carboxy, carbamyl, aryl, or heterocyclo; and

R₄, R₅, and R₉ are hydrogen.

- 5 54. The method of claim 53, wherein R₃ is -CH₃, -CH₂CH₃, -OCH₂CH₃, -F, -Br, -CF₃, -CBr₃, -OH, -O-CH₂-CH=CH₂, -CH₂-CH₂=CH₂, -NH₂, -NO₂, -cyano, -carboxy, or -benzyl.
55. The method of claim 49, wherein said vascular proliferative disorder is selected from the group consisting of solid tumor cancer, wet age-related macular degeneration, diabetic retinopathy, retinopathy of prematurity, diabetic macular edema, uveitis, corneal neovascularization, psoriasis, rheumatoid arthritis, atheroma, restenosis, Kaposi's sarcoma, haemangioma, and inflammatory diseases characterized by vascular proliferation.
- 10 56. The method of claim 49, wherein the reduction in blood flow causes the occlusion, destruction, or damage of proliferating vasculature.
- 15 57. A composition selected from the group consisting of 6-[(Z)-2-(3,4,5-Trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 3-Ethyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene 3-Methyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Bromo-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Phenyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 3-Allyl-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 4-Fluoro-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-1,2-dihydroxybenzene, 2,3,4-Trihydroxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 2,3-Dihydroxy-4-ethoxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 2,3-Dihydroxy-4-allyloxy-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-benzene, 4-Nitro-6-[(Z)-2-(3,4,5-trimethoxyphenyl)vinyl]-2,3-dihydroxybenzene, 2',3'-dihydroxy-3,5-dichloro-4,4'-dimethoxy-(Z)-stilbene, 2',3'-dihydroxy-4'-methoxy-3,4,5-trifluoro-(Z)-stilbene, 2,3-Dihydroxy-4-methoxy-[(Z)-2-(3,4,5-trimethoxyphenyl) Beta lactam]-benzene, 2',3' diphosphate-3,4,5-trimethoxy-(Z)-stilbene, tetrasodium salt; 3',4' diphosphate-3,4,5-trimethoxy-(Z)-stilbene, tetrasodium salt; and combinations thereof.
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